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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,700	03/13/2001	Robert D. Ladner	266/176	1989

34055 7590 11/18/2002

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EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 11/18/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,700	LADNER ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 11 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The response to restriction requirement (Paper No. 13) filed on October 30, 2002 has been entered and considered.
2. The Information Disclosure Statement (Paper Nos. 3) filed on July 30, 2001 and the Preliminary Amendment (Paper No. 10) filed on April 25, 2002 have been entered and considered.
3. Applicant's election without traverse of Group I (claims 1-10) in Paper No. 13 is acknowledged. Applicants' request for rejoinder of claims 11-12, drawn to method of treatment and the product is considered and found not persuasive because the claims drawn to the product and method of treating a patient are classified in separate class and subclass as compared to method claims in Groups I. Applicants' argument regarding the specific patents as an evidence to undue burden, is fully considered but found not persuasive because classification is prime basis for restriction which has not been rebutted simply because rejoinder may have occurred in some other cases does not eliminate the burden in this case. Each case is examined on its own merits and Group I is directed to a method of determination of uracil misincorporation into DNA by a test compound, whereas Group II is directed to a product (kit). The method steps are not necessary to practice the invention in Group II. Further (i) the issues are not the same with respect to 35 U.S.C.112 and 35 U.S.C. 101 statutes, (ii) separate Art Units would examine the two Groups under ordinary circumstances. Thus the restriction requirement is still deemed proper.
4. Claims in Group I are considered for examination in this office action. Claims 11-12 are withdrawn from further consideration.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gouliau et al (Proc.Natl.Acad.Sci.USA., Vol.77, No.4, pp 1956-1960, 1980) and in view of Gadsden et al. (EMBO J., vol.12, No.11, pp 4425-4431, 1993).

Gouliau et al. teach a method for determining if a test compound (methotrexate) induces uracil misincorporation into DNA wherein Gouliau et al. disclose that the method comprises (a) providing the wild type cells (human lymphoid cells), (see page 1956, column 2, paragraph 1); (b) exposing the cells to an agent that directly or indirectly inhibits thymidylate metabolism, in the presence or absence of the test compound (see page 1956, column 1, abstract, column 2, paragraph 1); (c) measuring amount dUTP in DNA of the said cells (see page 1957, column 1, paragraphs 1-5, column 2, paragraphs 1-2); (d) interpreting the measured parameter in treated

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and untreated cells which indicates cytotoxicity, elevated dUTP pools, impaired growth and viability no detectable levels of uracil indicates that the test compound induces uracil misincorporation into DNA (see page 1959, column 1, paragraphs 1-2, column 2, paragraphs 1-2). Gouliau et al. also teaches (i) reduction in dUTPase in cells treated with a test drug or compound (see page 1959, column 2, paragraph 3); (ii) the conversion of dUMP to TMP is inhibited by antifolate consisting of aminopterin (methotrexate) (see page 1956, column 1, paragraph 3); and (iii) comprises two test compounds (methotrexate and FdUrd) (see page 1959, column 2, paragraph 1). However Gouliau et al. did not teach providing cells overexpressing dUTPase or uracil-DNA glycosylase or uracil-DNA glycosylase inhibitor protein.

Gadsden et al. teaches dUTP pyrophosphatase (dUTPase) as an important enzyme for cell viability and demonstrated the role of dUTPase in the life cycle of yeast cells (see page 4425, column 1, abstract). Gadsden et al. also disclose a method comprising dUTPase expressing cells (EM932), uracil-DNA glycosylase (dut^-) expressing cells and uracil glycosylase inhibiting cells (tup^-) (see page 4430, column 2, paragraphs 1-5, page 4428, column 1, paragraphs 1-2, column 2, paragraphs 1-2, page 4429, column 2, paragraphs 1-2). Further, Gadsden et al. disclose (i) cytotoxicity induced by deficiency of dUTPase in cells (see page 4428, column 2, paragraph 2); (ii) comparison of these different cells in measuring cell viability, uracil incorporation, cell cycle arrest (see page 4427, column 2, paragraph 1, page 4428, column 1, paragraph 2, column 2, paragraphs 1-2); and (iii) uracil-DNA glycosylase could be obtained from human, drosophila, or a virus (see page 4430, column 1, paragraph 2).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method of determining uracil misincorporation

into DNA as taught by Goulian et al. with the cells expressing dUTPase / uracil-DNA glycoylase as taught by Gadsden et al. to achieve expected advantage of developing a sensitive method for characterizing uracil misincorporation into DNA because Gadsden et al. suggests that "the findings that dUTPase is essential for DNA replication in yeast supports the contention that inhibitors of the human enzyme may be useful as chemotherapeutic compounds. Further, inhibitors of uracil glycosylase used in combination with agents that block dihydrofolate reductase or thymidylate synthase should promote the stable substitution of uracil for thymine in DNA during replication." (see page 4430, column 1, paragraph 2). An ordinary practitioner would have been motivated to combine the method of Goulian with the method of Gadsden et al. to enhance the sensitivity of the assay by incorporating the additional parameters to support the uracil misincorporation into DNA because the comparison of different parameters in different cells would result in a better profile for characterization of a test compound and its role in misincorporation of uracil into DNA.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-305-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.


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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Suryaprabha Chunduru
November 14, 2002


JEFFREY FREDMAN
PRIMARY EXAMINER